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An Interview With Dr. Lewis Thomas

The Road to Research

Along the tile corridor of the sixth floor of Memorial Sloan-Kettering Cancer Center in New York City stand cylinders of compressed gas, portable trays on wheels, metal stands holding plastic jugs of colorless liquids, and cabinets filled with beakers, glasses, and boxes of chemicals. One passes labs with glass tubing and glowing Bunsen burners, refrigerated labs behind metal doors, and white-coated men and women. At the end of the hall is the office of Dr. Lewis Thomas, chancellor of the institute as well as the author of such renowned books as *The Lives of a Cell*, *The Medusa and the Snail*, and, most recently, *The Youngest Science, Notes of a Medicine-Watcher*.

Dr. Thomas is a soft-spoken scientist whose outward calm belies his invigorating mind. As he discusses issues facing the scientific and business communities, he chooses to focus on what he calls the "intellectual connections" between the two fields, particularly the shared concerns about basic and applied research.

His thoughts come slowly, softly. His fingers move gently, cupping a cigarette, twirling tortoise shell glasses, cradling his jaw as he speaks. The following is an edited version of a recent conversation.

You have said that you are not sure that the term "high technology" could be applied to the biomedical field. Would you care to explain?

What I meant is that I don't regard machinery, such as a CAT scanner or the artificial heart, as representing high technology. I think today's version of high technology in the biomedical field is the working out of techniques for manipulating DNA *in vivo*. Recombinant DNA is an advance that I would regard as the greatest thing that has ever happened in biological science. It is now possible for cell biologists and immunologists and molecular geneticists to get

answers that were inconceivable just a few years ago. I think that when historians one day write about the biological revolution, they'll date it in the past decade.

The significance of recombinant DNA technology is that we can now begin to look at events not just inside the cell but inside the intricate machinery of these cells, and this means to me that we ought to be able to explore disease mechanisms in a way we've never been able to do before. This is why I'm so optimistic about our being able to do something decisive with the problem of cancer in some sort of real time. The work is moving very fast, and the investigators who are doing this work are extremely enthusiastic, highly competent, and pretty sure that before long they're going to understand what goes on at a deep level in cancer. And when that happens, it is likely that we will be able to devise either pharmacological or immunological approaches that we would not have been able to come up with otherwise.

So the great need in medicine is for more basic biomedical research, and I would like to talk about something fascinating that is happening today in this field.

What do you see taking place?

Well, there are new connections being made between industrial science and academic science. It used to be that industrial science—or applied science—was targeted toward a product, while what went on in the university world was largely basic science that was aimed at acquiring an understanding of the mechanisms in nature. And there was no connection between those two communities. A few decades ago, this changed in the physical sciences, as institutions like MIT and Cal-Tech began working with the industrial world, and some major corporations began

investing in basic science in the universities. But this didn't happen in biomedical science until recently.

Why did it happen in the other fields and not in medicine?

I think it became quite clear after World War II that there were problems of deep concern to the corporate world which could be solved only by making use of the basic science information being generated in the university laboratories. I don't know why it didn't happen simultaneously in biomedical science. Perhaps it was because the academic people felt that any connection to industry and the marketplace would somehow contaminate them and lead them away from their primary objective of understanding the mechanisms of nature. I think, though, that the main problem was that the two communities simply existed apart from each other. They didn't go to the same meetings, didn't belong to the same societies. And the change has come about because there has been a revolution in science in the academic world. It became clear to everybody that there would be practical applications of this new science, and the corporate world was interested.

But it should also be said that the university world no longer has a feeling of apprehension about intellectual contact with the corporate world. I could cite the Hoechst contract with Massachusetts General Hospital that provides a large sum of money over 20 years to support pure basic research in molecular genetics. There is no requirement that the Harvard scientists in the Mass. General laboratories choose a line of research that would be of special interest to a pharmaceutical house, much less any obligation to produce a product. The only quid pro quo I'm aware of is that the corporation gets the first look at the basic science as it comes out, and if it looks interesting they have the first option to turn it into a product.

There are similar arrangements between Du Pont and the Harvard Medical School, as well as Johnson and Johnson and the Scripps Clinic and Research Foundation in California—plus a good many others now on-line. Now, I can't imagine that such a partnership with industry could ever cover more than 10 percent of a lab's research costs, but what it does is provide long-term support that the government doesn't provide. Government support comes in two-year awards from the National Institutes of Health (NIH), and the young investigators feel these days that they are in a very unstable environment if they depend entirely on NIH grants. In fact, there has been a recent tendency to take on research problems that look absolutely sound and which promise results within 12 to 18 months. So the new arrangements with industry mean that the investigators don't need to be apprehensive about their salaries and can undertake longer-term approaches to research. And the ability to gamble in the laboratory is what has made American science the best science on earth.

So you are comfortable with these new financial resources.

Yes, but I'm worried, too. I'm worried that sooner or later we may start neglecting some fields of science. I sense a belief in Washington that there is not enough money to do basic research across the board in biology, in physics, in chemistry, and so we should support these fields which look as though they have some promise for the 1990s. I see a great danger in committees sitting down and trying to figure out what's going to be important 10 or 20 years from now. It would never have crossed anyone's mind in the 1960s what we are able to do today in manipulating genes, of inserting genes from one kind of cell into a different cell. What we had was a lot of research in molecular biology being done just because it was fascinating to young scientists.

Science, you're saying, is built on long-range thinking.

Not in research itself, not at all. Basic research is done by people who want quick answers to engrossing questions. But they are also aware of two other things. First, your original guess is probably going to turn out to be wrong. You can write a 100-page application to NIH saying exactly what you're going to do the next two years; but if you're a good investigator, you'll put that aside as soon as you start, because you're going to notice things you hadn't expected to see and soon find yourself in a different world. The second lesson is that you never finish. As soon as you reach what you think is the final answer to a problem, it stops becoming a final answer and becomes an array of new questions. So in that sense you could say it is long-range thinking.

Who has changed, then, the basic scientist or the applied scientist, as they now work together?

Well, it comes back to both sides realizing that you're not going to get any applied science solutions falling into your lap without a lot of basic inquiry happening beforehand. I think we in the academic world have tended to look down our noses at industrial science in the past as not pure science but just a way of making money. And now there are some very amiable and exciting relationships beginning to start up between these two scientific worlds; and, if handled carefully, this could be a wonderful thing for our country. It could put us in a better competitive position with both Europe and Japan, where there's a closer connection between applied and basic science.

What do you mean, handled carefully?

There is anxiety in the university world over the issue of confidentiality and secrecy—that the needs for patents and licensing will delay information coming out of the basic research laboratory. But I think that if the information is patentable, it will not take all that time to get the machinery cranked up. So I don't see a restraint on publication. What I am worried about is that there may be less free gossiping in the halls of university science. When the bright investigators I know run into something interesting in their lab, they

can't wait until lunch time to tell everyone else. And this communication system based on phone calls, corridor gossip, and international meetings is very effective. So I worry that investigators may think that if they tell what is going on in their laboratory, someone else may pick it up, and they'll lose their priority on it. It's not something to worry about now, but we should be apprehensive about it in the future.

Do you think the public understands how basic science works?

No. In fact, I think the public worries about what scientists may be doing to the world. They associate technology—such as for thermonuclear weapons—with science much more closely than they should. Technology is one thing, and science is another. Society, through its elected officials, certainly ought to choose between what technology it wants and what it doesn't want; but, as I said, you can't make choices in basic science. There aren't any questions that should be disallowed, because you can't predict how the inquiry is going to turn out.

Even when there is apprehension, such as that concerning genetic engineering?

Well, we've had a long run now in molecular genetics—almost 10 years—since the scientists themselves first cited the possible dangers of gene transfers. So there was a moratorium for a while, and a lot of guidelines were established by the NIH which are still in effect; and there's been no evidence of any accident, not even of any risk. Quite clearly, nothing has gone wrong. There's a general agreement now within the scientific community that such research applications as interferon and the cloning of genetic information essentially carry no risk at all. But there is still a feeling in the public mind that fooling around with the genome is something we ought not to be doing.

The genome?

That's jargon for the entire genetic machinery in the nucleus of the cells. The interest, you see, lies in replacing DNA that may be congenitally lacking in cells; for when it is, some people don't have the right enzymes that are essential for life. And while it can't be done now, replacing that DNA information sometime in the future could save the lives of children who would otherwise die. But I don't think this so-called genetic engineering will ever be applied to the germ plasm itself.

Out of choice or the lack of technology?

Both. It's a complicated ethical question, really, and I don't see much interest in the scientific community to go ahead with this kind of work. I can't imagine anybody in science ever wanting to become involved in the cloning of a human being, for example, even if one day it could be done. Besides, it would require the whole GNP just to support the research, because you'd have to clone parents, grandparents, aunts, uncles, cousins—the entire environment—and that's a

science fiction invention. I think that what is needed is a better case made by the scientific community for what is going on in basic research. The main thing that is happening is that we're beginning to understand how life works. When people look back at the twentieth century, the most important discovery of science may be that we learned how little we know about our origins, about how our minds work, and how we live together. In preceding centuries we thought we knew everything; in this century, we have discovered through science how ignorant we are.

It sounds like there is a communications gap here. Is it not difficult for science to communicate its potential to the public?

Yes, and one of my preoccupations these days is to help the general literate public understand what is going on in science. So I am helping to develop a series of books by working scientists. They will be on everything from galactic cosmology to molecular genetics. What happened, for example, during that major portion of the earth's existence up to a billion years ago when there was nothing but bacteria and perhaps their viruses? Biological habits originated then that have persisted. Another subject is clinical science. How do you actually do research with human patients? What are the objectives? What ethical problems exist?

Are there going to be certain scientific discoveries down the road that confront us with ethical decisions?

We scientists may have to confront some ethical choices. For example, there's something about cloning individuals that I myself find a plain violation of the human spirit—it would be wrong. I would take a stand that it should be forbidden. But even in that case it would not be science itself that would raise the ethical question; it would be the *application* of the science that would do so. Let's take a more realistic possibility—that we will be able to transplant human organs with ease. That also is technology, and whether or not to spend money on basic science to make that possible should be a public decision. It should not be a decision made by doctors or biomedical scientists. It should be made by Congress and the people.

Would you sum up your thoughts about the basic and applied sciences, and the role of research in our society?

We are an industrial society, and the whole world is becoming one as well. If we are going to be successful in developing the technologies that we need in order to survive as a species, we need to be totally dependent on basic research. The topmost priority in the United States of America ought to be the fostering of a fundamental inquiry into nature, without imposing targets, without trying to choose between fields. Research in marine biology should be just as important as research on human DNA, and that extends to laser communications, to artificial intelligence, to all physics, chemistry, and the biological sciences. I think we can afford it. I know we're good at it, and we ought to be enlisting our brightest young people to do it. I think the future depends on it. ▲